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- 81. Maxam and Gilbert, <u>Proc. Nat. Acad. Sci.</u> 74, 560 (1977).
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- 83. Itakura <u>et al.</u>, <u>Science</u> <u>198</u>, 1056 (1977).
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## IN THE CLAIMS:

Please cancel claims 1, 6, 9-17, and 24-25, without prejudice.

## Please amend the remaining claims as follows:

A. (Amended) A process for obtaining a <u>mature</u> protein heterologous to yeast as a product of yeast expression, which process comprises:

(a) transforming a yeast organism with an expression vehicle comprising [the] a DNA sequence encoding [substantially the] an Arg C-terminal pre-pro peptide of yeast alpha factor operably connected in translation reading frame without intervening Glu (or Asp)-Ala dipeptide repeats to a DNA sequence encoding a mature protein heterologous to the yeast organism;

(b) culturing the transformed organism; and

(c) recovering the <u>mature</u> protein from the culture.

(Amended) A process for obtaining a <u>mature</u> protein heterologous to yeast as a product of yeast expression, processing and secretion, which process comprises:

(a) transforming a yeast organism with an expression vehicle comprising [the DNA sequence of the promoter] yeast alpha factor promoter DNA sequence operably linked to [substantially the] an Arg C-terminal pre-pro peptide sequence of [the] yeast alpha factor

[gene] which is operably connected in translation reading frame without intervening Glu (or Asp)-Ala dipeptide repeats to a DNA sequence encoding a mature protein heterologous to the yeast organism;

- (b) culturing the transformed yeast organism; and
- (c) recovering the mature protein from its supporting medium.
- 4. (Amended) A process for secreting a <u>mature</u> protein heterologous to yeast into the supporting medium, which process comprises:
- (a) transforming a yeast organism with an expression vehicle comprising [the] a DNA sequence encoding [substantially the] an Arg C-terminal pre-pro peptide of yeast alpha factor, operably connected in translation reading frame without intervening Glu (or Asp)-Ala dipertide repeats to a DNA sequence encoding a mature protein heterologous to the yeast organism; and
  - (b) culturing the transformed organism.
- 5. (Amended) The process of Claim 4 wherein said DNA [sequences are] sequence encoding an Arg C-terminal pre-pro peptide of yeast alpha factor is under the control of alpha factor promoter.

An expression vehicle [of Claim 6 which also includes the] comprising yeast alpha factor promoter DNA sequence operably connected to a DNA sequence encoding a mature protein heterologous to the yeast organism, and also comprising a DNA sequence encoding [substantially the] an Arg C-terminal pre-pro peptide of yeast alpha factor operably linked in translation reading frame without intervening Glu (or Asp)-Ala dipeptide repeats upstream to the DNA sequence encoding [a] the mature protein heterologous to the yeast organism, wherein the protein is in discrete form unaccompanied by any substantial peptide

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presequence or other artifact of expression, as a product of yeast expression, processing and secretion.

8. (Amended) A yeast expression vehicle comprising [the] a DNA sequence encoding [substantially the] an Arg C-terminal pre-pro peptide of yeast alpha factor [gene] operably connected in translation reading frame without intervening Glu (or Asp)-Ala dipeptide repeats to a DNA sequence encoding a mature protein heterologous to the yeast organism, wherein the protein is in discrete form unaccompanied by any substantial peptide presequence or other artifact of expression, as a product of yeast expression, processing and secretion.

18. (Amended) The expression vehicle of Claim 7 wherein the DNA sequence encoding [heterologous] the mature protein heterologous to the yeast organism encodes [for a protein selected from the group consisting of] human interferon [, bovine interferon, tissue plasminogen activator, and rennin].

19. (Amended) The expression vehicle of Claim 8 wherein the DNA sequence encoding [heterologous] the mature protein heterologous to the yeast organism encodes [for a protein selected from the group consisting of] human interferon [, bovine interferon, tissue plasminogen activator, and rennin].

In claim 22, line 1, change "transformed with" to --comprising.

In claim 23, line 1, change "transformed with" to --comprising.

Please add new claims as follows:

- --26. The expression vehicle of Claim 7 wherein the DNA sequence encoding the mature protein heterologous to the yeast organism encodes bovine interferon.--
- --27. The expression vehicle of Claim 7 wherein the DNA sequence encoding the mature protein heterologous to the yeast organism encodes tissue plasminogen activator.--
- --28. The expression vehicle of Claim 7 wherein the DNA sequence encoding the mature protein heterologous to the yeast organism encodes rennin.--
- --29. The expression vehicle of Claim 8 wherein the DNA sequence encoding the mature protein heterologous to the yeast organism encodes bovine interferon.--
- --30. The expression vehicle of Claim 8 wherein the DNA sequence encoding the mature protein heterologous to the yeast organism encodes tissue plasminogen activator.--
- --31. The expression vehicle of Claim 8 wherein the DNA sequence encoding the mature protein heterologous to the yeast organism encodes rennin.--
- --32. A DNA molecule comprising a DNA sequence encoding an Arg C-terminal pre-pro peptide of yeast alpha factor operably connected in translation reading frame without intervening Glu (or Asp)-Ala dipeptide repeats to a DNA sequence encoding a mature protein heterologous to the yeast organism.--
- -- 33. The DNA molecule of claim 32 wherein the DNA sequences are under the control of alpha factor promoter.--

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- --34. The DNA molecule of claim 32 wherein the DNA sequence encoding the mature protein heterologous to the yeast organism encodes insulin-like growth factor.--
- --35. The DNA molecule of claim 32 wherein the DNA sequence encoding the mature protein heterologous to the yeast organism encodes human interferon.--
- --36. The DNA molecule of claim 32 wherein the DNA sequence encoding the mature protein heterologous to the yeast organism encodes boyine interferon.--
- -37. The DNA molecule of claim 32 wherein the DNA sequence encoding the mature protein heterologous to the yeast organism encodes tissue plasminogen activator.--
- --38. The DNA molecule of claim 32 wherein the DNA sequence encoding the mature protein heterologous to the yeast organism encodes rennin.--
- --39. The process of claim 2 wherein the DNA encoding all of the Gly (or Asp)-Ala dipeptide repeats has been deleted from the pre-pro peptide of the yeast alpha factor DNA--.
- --40. A process for obtaining a mature protein heterologous to yeast as a product of yeast expression, which process comprises:
- (a) culturing a yeast organism comprising an expression vehicle comprising a DNA sequence encoding an Arg C-terminal prepro peptide of yeast alpha factor operably connected in translation reading frame without intervening Glu (or Asp)-Ala dipeptide repeats to a DNA sequence encoding a mature protein heterologous to the yeast organism; and
  - (b) recovering the mature protein from the culture .--

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- -- Al. A process for obtaining a mature protein heterologous to yeast as a product of yeast expression, processing and secretion, which process comprises:
- (a) culturing a yeast organism comprising an expression vehicle comprising yeast alpha factor promoter DNA sequence operably linked to an Arg C-terminal pre-pro peptide sequence of yeast alpha factor which is operably connected in translation reading frame without intervening Glu (or Asp)-Ala dipeptide repeats to a DNA sequence encoding a mature protein heterologous to the yeast organism; and
- (b) recovering the mature protein from its supporting medium.--
- --42. A process for secreting a mature protein heterologous to yeast into the supporting medium, which process comprises culturing a yeast organism comprising an expression vehicle comprising a DNA sequence encoding an Arg C-terminal pre-pro peptide of yeast alpha factor, operably connected in translation reading frame without intervening Glu (or Asp)-Ala dipeptide repeats to a DNA sequence encoding a mature protein heterologous to the yeast organism.--
- --43. The process of claim 40 wherein said DNA sequence encoding an Arg C-terminal pre-pro peptide of yeast alpha factor is under the control of alpha factor promoter.--
- --44. The process of claim 42 wherein said DNA sequence encoding an Arg C-terminal pre-pro peptide of yeast alpha factor is under the control of alpha factor promoter.--
- --45. The process of claim 2 wherein said DNA sequence encoding an Arg C-terminal pre-pro peptide of yeast alpha factor is under the control of alpha factor promoter.--

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